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EXAMINER

DAVIS, KATHARINE F

ART UNIT	PAPER NUMBER
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1636

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Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/713,794

Applicant(s)

BATARD ET AL.

Examiner

Katharine F. Davis

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 15 November 2000.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-28 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-28 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

### Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☒ Certified copies of the priority documents have been received in Application No. 09/158,767.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                  | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____  |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                         | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>3</u> . | 6) <input type="checkbox"/> Other:  |

### **DETAILED ACTION**

This Office Action is in response to the application (including Preliminary Amendment) filed on November 15, 2000. Claims 1-28 are pending in the instant application.

#### ***Information Disclosure Statement***

It is noted that document number 5 listed in the non-patent document section of the Information Disclosure Statement filed on November 15, 2000 has not been considered because this document contains a hyperlink. Hyperlinks are not considered to be prior art documents. This information can be re-submitted in a format that does not have a hyperlink.

#### ***Specification***

The abstract of the disclosure is objected to because it contains more than the one required paragraph. Correction is required. See MPEP § 608.01(b).

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see page 3, line 22). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

#### ***Claim Objections***

Claims 1-28 are objected to because of the following informalities:

Claims 1-28 are objected to for not beginning with an article, for example, "A DNA sequence..."

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Claims 20 and 21 are objected to for referring to sequences with "ID NO" rather with the proper "SEQ ID NO".

Claim 21 is objected to for referring to one of a DNA sequence encoding a cytochrome P-450 with SEQ ID NOS:7, 8, 9, or 13 wherein SEQ ID NO:13 is not a cytochrome P-450 it is a reverse primer (see the Sequence Listing and Example 4 in the specification). It is assumed for the purpose of examination that SEQ ID NO:13 should be replaced with SEQ ID NO:14.

### ***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-8 and 12-23 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 1-8 and 12-23 read on sequences which can be interpreted to be naturally occurring sequences. Products of nature are not patentable. Amending the claims to read, for example "An isolated DNA sequence..." would overcome this rejection.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claims 1-28 are indefinite as it is unclear from the claim language what sequences are actually being claimed; the sequences which contain codons that are poorly suited to yeasts or the sequences which contain replaced codons?

Claims 1-28 are indefinite in the recitation of the phrases "...a sufficient number of codons..." and a "sufficient number" of CTC codons or CTC and CTG codons. It is unclear what constitutes a "sufficient number" of codons, thus rendering the metes and bounds of the claims undetermined. It is assumed for the purposes of examination that a sufficient number of codons refers to a number sufficient to allow expression of the claimed DNA sequences in yeast.

Claims 1-8 and 12-28 are indefinite in the recitation of the phrases "poorly suited to yeasts" and "well suited to yeasts". The boundary between poorly suited and well suited is unclear. It is assumed for the purposes of examination that poorly suited codons would not allow expression in yeast and well suited codons allow expression in yeast.

Claims 1-8 and 12-28 are indefinite for recitation of the phrase "corresponding codons", as it is unclear whether corresponding refers only to the position of the codon within the DNA sequence or to synonymous codons coding for the same amino acid. For the purpose of examination it is assumed that "corresponding codons" means synonymous codons coding for the same amino acid.

Claims 2-8 and 12-28 are indefinite for the recitation of phrases such as "whose frequency of use by yeasts is greater than 15 per 1000, **or** greater than or equal to 20 per 1000, **or** "whose frequency of use by yeasts is less than or equal to approximately 13 per 1000, **or** less than or equal to approximately 12 per 1000". The unit of the denominator in these fractional

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comparisons is unclear. For the purpose of examination it is assumed to mean frequency of use per 1000 codons.

Claims 9-11 are indefinite for the recitation of the phrase "high content of leucine" as it is unclear what constitutes a high content of leucine thereby rendering the metes and bounds of the claims undetermined.

Claims 13-19, 21 and 25-27 are indefinite for the recitation of phrases "...characterized in that it..." The antecedent basis for "it" is vague in the claims.

Claims 2-6, 12, 15-17 and 26 are indefinite for reciting a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation in the same claim.

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 2 recites the broad recitation "less than or equal to approximately 13 per 1000", and the claim also recites "less than or equal to approximately 10

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per 1000", which is the narrower statement of the range/limitation; claim 5 recites the broad recitation "greater than 15 per 1000", and the claim also recites "greater than or equal to 20 per 1000", which is the narrower statement of the range/limitation and claim 12 recites the broad recitation "at least 30 percent", and the claim also recites "at least 20 percent", which is the narrower statement of the range/limitation. In the present instance, claims 15, 16, 17 and 26 recite the broad recitations; an isolated DNA sequence of natural origin, dicotyledonous or monocotyledonous plants, plants of the gramineae family and genera *Saccharomyces*, *Kluyveromyces*, *Hansenula*, *Pichia*, and *Yarrowia*, respectively and the claims also recite in particular of plant origin, in particular from monocotyledonous plants, in particular from among wheat, barley, oats, rice, maize, sorghum and cane sugar and advantageously from the genus *Saccharomyces*, in particular *Saccharomyces cerevisiae*, respectively which are the narrower statements of the range/limitations in claims 15, 16, 17 and 26.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8, 12, 13, 18 and 22-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Hoekema *et al.* (Molecular and Cellular Biology 7:2914-2924 1987). Hoekema *et al.* teach a genetic manipulation of the enzyme phosphoglycerate kinase (PKG1) from *Saccharomyces cerevisiae* wherein the manipulation comprises codon replacement, for example replacement of

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codons which are well suited for expression in yeast with codons that are poorly suited for expression in yeast in order to assess the effect of codon bias on gene expression. The codon replacement method of Hoekema *et al.* displays the limitations as recited in the instant claims 2-6 in Table 1 and Figure 1A on page 2916, for example, poorly suited (minor) codons for expression in yeast are selected from CTC which encodes leucine (figure 1A), CGG (arginine), GCG (alanine), GGA (glycine), and CCG (proline) as shown in Table 1. Codons which are well suited for expression in yeast are also shown in Table 1, for example CCA (proline). Table 2 on page 2917 shows that sequence regions with a high content of codons which are poorly suited for expression in yeast contain at least two poorly suited codons among ten consecutive codons and higher than two in most regions. Table 2 (see also the abstract) shows that Hoekema *et al.* implicated their method of codon replacement in the 5' region of the PGK1 gene. Hoekema *et al.* also teach a process for transforming yeast (*Saccharomyces cerevisiae*) with a chimeric plasmid encoding the PGK1 gene comprising the codon replacements (see entire article, especially Figure 4). Hoekema *et al.* additionally teach yeast cells (*Saccharomyces cerevisiae*) transformed by their method. Claims 1-8, 12, 13, 18 and 22-26 read on the sequences, genes, vectors, methods and transformed yeast of Hoekema *et al.*

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.



This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 15-17 and 27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoekema *et al.* in view of Neill *et al.* (Gene 55:303-317 1987). Hoekema *et al.* is applied as above in the 102(b) rejection. However Hoekema *et al.* does not teach sequences from plants nor does Hoekema *et al.* teach a process for producing a heterologous protein of interest in a transformed yeast cell. Neill *et al.* teach a method for expression of wheat  $\alpha$ -gliadin in *Saccharomyces cerevisiae* (see abstract and page 313, section e). Both the teachings of Hoekema *et al.* and Neill *et al.* were known in the art at the time that the instant invention was made and one of ordinary skill in the art would be familiar with these teachings. Accordingly as ordinary skilled artisans were already practicing the expression of plant sequences in yeast at the time that the instant invention was made; the ordinary skilled artisan would have been motivated to optimize expression of these sequences. The method of Hoekema *et al.* uses codon manipulation to optimize expression in yeast. Thus it would have been obvious to one of ordinary skill in the art at the time that the instant invention was made to use the methods of Hoekema *et al.* to optimize expression of plant sequences in yeast. Given the teachings of the cited prior art and given the level of skill of the ordinary artisan at the time that the instant invention was made,

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said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 19 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoekema *et al.* in view of Skaggs *et al.* (Gene 169:105-109 1996, IDS reference). Hoekema *et al.* is applied as above in the 102(b) rejection. However Hoekema *et al.* does not teach an enzyme sequence that encodes a cytochrome P450 nor does Hoekema *et al.* teach a process for transforming a substrate by enzyme catalysis using an enzyme that is expressed in a yeast. Skaggs *et al.* teach a DNA sequence encoding a cytochrome P450 involved in ergosterol biosynthesis from the yeast *Saccharomyces cerevisiae* (see Figure 3). Further Skaggs *et al.* teach introduction of the yeast cytochrome P450 sequence into a yeast integrating vector, yeast transformed with the vector, and functional expression of the yeast cytochrome P450 DNA as evidenced by rescue of a yeast mutant with regard to its ergosterol synthesis (see page 107, part c). The rescue of the yeast mutant in the method of Skaggs *et al.* is shown by assay of the sterol profile which involves recovering a substrate transformed by enzyme catalysis (see Figure 1). Both the teachings of Hoekema *et al.* and Skaggs *et al.* were known in the art at the time that the instant invention was made and one of ordinary skill in the art would be familiar with these teachings. One of ordinary skill in the art would realize that the study of enzyme function can help to elucidate many biosynthetic pathways and would be familiar with the advantages of using yeast expression systems to study protein function. One of ordinary skill in the art would be motivated to manipulate sequences encoding proteins for optimal expression in these yeast systems. Thus it would have been obvious to one of ordinary skill in the art at the time that the

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instant invention was made to use the codon manipulation taught by Hoekema *et al.* to optimize expression of enzyme sequences in yeast in order to efficiently study enzyme functions. Given the teachings of the cited prior art and given the level of skill of the ordinary artisan at the time that the instant invention was made, said ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

### *Conclusion*

Claims 1-28 are rejected. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Katharine F. Davis whose telephone number is (703) 605-1195 with direct desktop RightFax (703) 746-5199. The examiner can normally be reached on Monday-Friday (8:30am-5:00pm). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached on (703) 305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 305-1935 for After Final communications. Any inquiry of a general nature or any inquiry concerning the formalities of this application should be directed to Patent Analyst Tracey Johnson whose telephone number is (703) 305-2982.

Katharine F. Davis  
March 19, 2002

DAVID GUZO  
PRIMARY EXAMINER  
